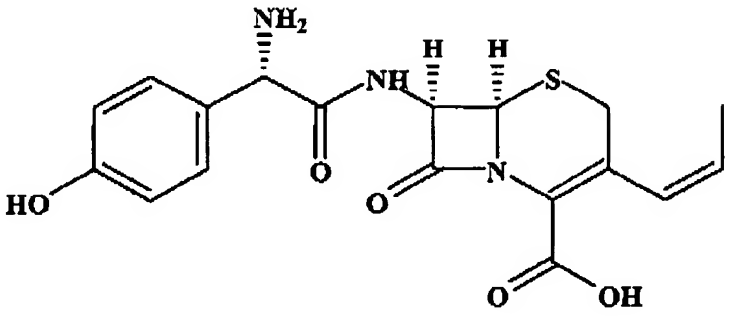
App. No.: 10/801,443
Art Unit: 1624

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

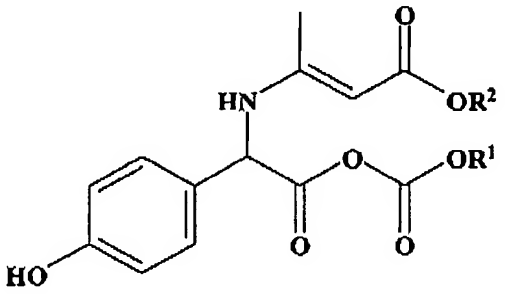
Listing of Claims:

1. (Currently Amended) A process for preparation of Cefprozil of formula (I)



(I)

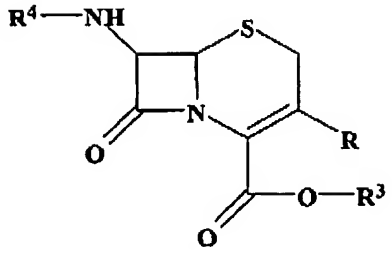
in the form of a monohydrate, the process comprising: ~~of reacting a~~
condensing a mixed acid anhydride of α-amino-p-hydroxy phenylacetic acid of formula (III)



(III)

wherein R^1 is an alkyl or an aryl group, and R^2 is methyl or ethyl,

with a protected 7-amino-3-(propen-1-yl)-3-cephem-4-carboxylic acid of formula (VII)



(VII)

wherein R^3 and R^4 are protective groups, and R is propen-1-yl,
followed by hydrolysis, isolation and purification to give Cefprozil of formula (I) in the form of a monohydrate ~~in high yield and purity, substantially free of impurities~~,

wherein the mixed anhydride of formula (III) is prepared by a process comprising the steps of

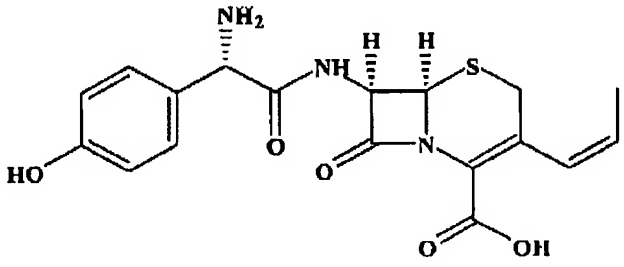
(a) adding a suitable acylating agent and a base to a mixture of an inert organic solvent and a polar aprotic solvent at a temperature in the range of 0° to 40°C;

(b) cooling the solution to a temperature in the range of –70° to –30°C;

(c) addition of Dane salt of an α-amino-p-hydroxy phenyl acetic acid to the cooled solution and agitation at a temperature in the range of –70° to –30°C.

2. (Canceled)

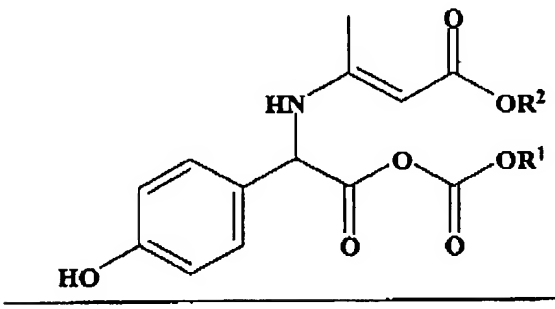
3. (Currently Amended) ~~A process as in claim 1~~A process for preparation of Cefprozil of formula (I)



(I)

in the form of a monohydrate, the process comprising:

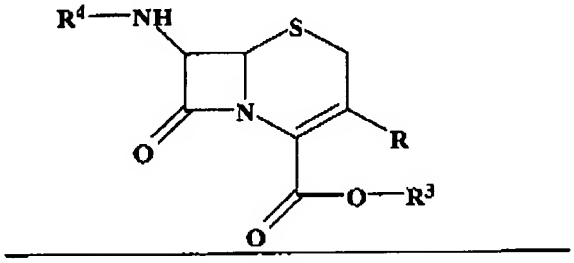
condensing a mixed acid anhydride of α-amino-p-hydroxy phenyl acetic acid of formula (III)



(III)

wherein R^1 is an alkyl or an aryl group and R^2 is methyl or ethyl,

with a protected 7-amino-3-(propen-1-yl)-3-cephem-4-carboxylic acid of formula (VII)



(VII)

wherein R^3 and R^4 are protective groups, R is propen-1-yl,

followed by hydrolysis, isolation and purification to give Cefprozil of formula (I) in the form of a monohydrate,

wherein the mixed anhydride of ~~an α-amino-p-hydroxy phenylacetic acid of~~ formula (III) is prepared by a process comprising the steps of

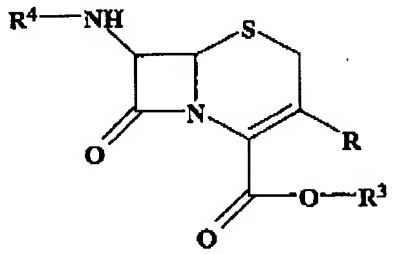
(a) adding [[an]] a suitable acylating agent and a base to an inert organic solvent at a temperature in the range of 0° to 40°C~~, preferably 20° to 25°C~~;

(b) cooling the solution to a temperature in the range of –70° to –30°C~~, preferably –35°C to –50°C~~;

(c) addition of Dane salt of an α-amino-p-hydroxy phenylacetic acid to the cooled solution and agitation at a temperature in the range of –70° to –30°C~~, preferably –35°C to –50°C~~;

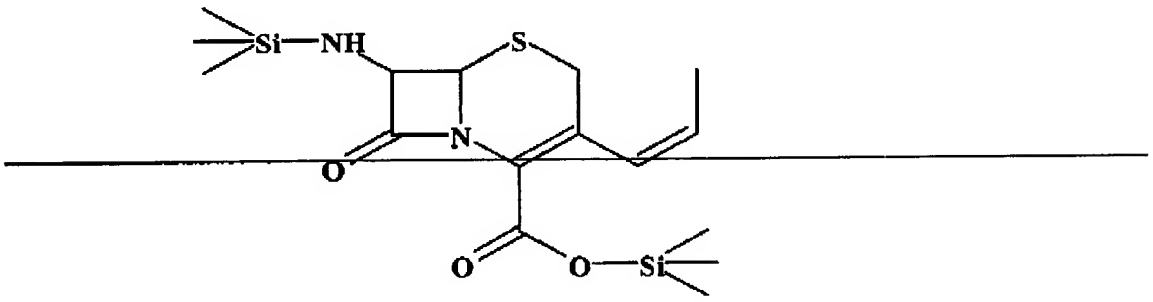
(d) addition of a polar aprotic solvent to the above solution and agitation at a temperature in the range of –70° to –30°C~~, preferably –35°C to –50°C~~.

4. (Currently Amended) A process as in claim 1 wherein the protected 7-amino-3-(propen-1-yl)-3-cephem-4-carboxylic [7-APCA] ~~7-APCA~~ of formula (VII) used



(VII)

is such that R^3 and R^4 are each a tri alkylsilyl group, ~~and represented by formula VI.~~



and R is propen-1-yl.

5. (Currently Amended) A process according to claim [[2]] 1, wherein the inert organic solvent employed in step [[i)]](a) is selected from the group consisting of methylene chloride,

tetrahydrofuran, chloroform, diethyl ether, chlorotethane, acetonitrile, trichloroethylene, and ethyl acetate.

6. (Currently Amended) A process according to claim 3, wherein the inert organic solvent employed in step [[i)]](a) is selected from the group consisting of methylene chloride, tetrahydrofuran, chloroform, diethyl ether, ~~chlorotethane~~ chloroethane, acetonitrile, trichloroethylene, and ethyl acetate.

7. (Currently Amended) A process according to claim [[2]] 1, wherein the polar aprotic solvent employed in step [[i)]](a) is selected from the group consisting of N, N-dimethyl formamide, acetone, acetonitrile, dimethyl sulphoxide, and dimethyl acetamide. ~~N,N-dimethyl formamide is the preferred polar aprotic solvent.~~

8. (Currently Amended) A process according to claim 3, wherein the polar aprotic solvent employed in step [[i)]](a) is selected from the group consisting of N, N-dimethyl formamide, acetone, acetonitrile, dimethyl sulphoxide, and dimethyl acetamide. ~~N,N-dimethyl formamide is the preferred polar aprotic solvent.~~

9. (Currently Amended) A process according to claim [[2]] 1, wherein the suitable acylating agent[[s]] employed in step [[i)]](a) is an ester of an ~~chosen from reactive forms of~~ aliphatic, alicyclic, or aromatic acid[[s]], or a halogenide of an aliphatic, alicyclic, or aromatic acid ~~such as chloroformic acid, benzoic acid, pivalic acid and 2-ethylhexanoic acid. The reactive forms of these acids include their esters such as ethyl chloroformate, isobutyl chloroformate and their halogenides like pivaloyl chloride, 2-ethyl hexanoyl chloride and benzoyl chloride, the preferred acylating agent being ethyl chloroformate~~.

10. (Currently Amended) A process according to claim 3, wherein the suitable acylating agent[[s]] employed in step [[i)]](a) is an ester of an ~~chosen from reactive forms of~~ aliphatic, alicyclic, or aromatic acid[[s]], or a halogenide of an aliphatic, alicyclic, or aromatic acid ~~such as~~

~~chloroformic acid, benzoic acid, pivalic acid and 2-ethylhexanoic acid. The reactive forms of these acids include their esters such as ethyl chloroformate, isobutyl chloroformate and their halogenides like pivaloyl chloride, 2-ethyl-hexanoyl chloride and benzoyl chloride, the preferred acylating agent being ethyl chloroformate~~.

11. (Currently Amended) A process according to claim [[2]] 1, wherein the base employed in step [[i)]](a) is selected from the group consisting of triethylamine, picoline, N-methylmorpholine, N, N-dimethylbenzylamine, lutidine, N, N-dimethyl-4-aminopyridine, and N, N-dicyclohexylamine~~, the preferred base being N-methylmorpholine~~.

12. (Currently Amended) A process according to claim 3, wherein the base employed in step [[i)]] (a) is selected from the group consisting of triethylamine, picoline, N-methylmorpholine, N, N-dimethylbenzylamine, lutidine, N, N-dimethyl-4-aminopyridine, and N, N-dicyclohexylamine~~, the preferred base being N-methylmorpholine~~.

13. (Currently Amended) A process according to claim [[2]] 1, wherein the acylating agent employed in step [[i)]](a) is ~~employed preferably~~ in the ~~range~~ molar ratio of [[1]] 1.0 to 1.5 moles per mole of Danc salt.

14. (Currently Amended) A process according to claim 3, wherein the acylating agent employed in step [[i)]] (a) is ~~employed preferably~~ in the ~~range~~ molar ratio of [[1]] 1.0 to 1.5 moles per mole of Dane salt.

15. (Currently Amended) A process according to claim [[2]] 1, wherein the base employed in step [[i)]](a) is ~~employed preferably~~ in the ~~range~~ molar ratio of 0.02 to 0.04 moles per mole of the Dane salt.

16. (Currently Amended) A process according to claim 3, wherein the base employed in step [[i)]](a) is ~~employed preferably~~ in the ~~range~~ molar ratio of 0.02 to 0.04 moles per mole of the Dane salt.

17. (Currently Amended) A process according to claim [[2]] 1 wherein the temperature in step [[i)]](a) is ~~preferably~~ in the range of 20° to 25°C.

18. (Currently Amended) A process according to claim 3 wherein the temperature in step [[i)]](a) is ~~preferably~~ in the range of 20° to 25°C.

19. (Currently Amended) A process according to claim [[2]] 1 wherein the Dane salt is ~~preferably~~ sodium or potassium D-N- (1-methoxycarbonylpropene-2-yl)-α-amino-p-hydroxyphenyl acetate or sodium or potassium D-N- (1-ethoxycarbonylpropene-2-yl)-α-amino-p-hydroxyphenyl acetate.

20. (Currently Amended) A process according to claim 3 wherein the Dane salt is ~~preferably~~ sodium or potassium D-N- (1-methoxycarbonylpropene-2-yl)-α-amino-p-hydroxyphenyl acetate or sodium or potassium D-N- (1-ethoxycarbonylpropene-2-yl)-α-amino-p-hydroxyphenyl acetate.

21. (Currently Amended) A process according to claim [[2]] 1 wherein the temperature in step [[i)(c)]] (b) is ~~preferably~~ in the range of -35°C to –50°C.

22. (Currently Amended) A process according to claim 3 wherein the temperature in step [[i)(c)]] (b) is ~~preferably~~ in the range of -35°C to –50°C.

23. (Currently Amended) A process according to claim [[2]] 1 wherein the temperature in step [[i)(d)]] (c) is ~~preferably~~ in the range of –35°C to –50°C.

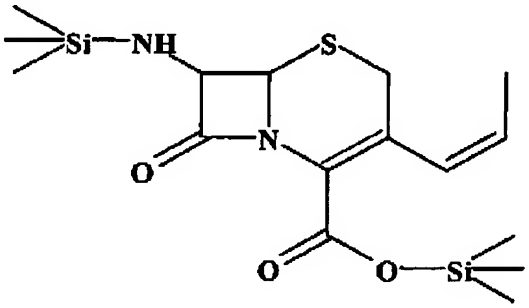
24. (Currently Amended) A process according to claim 3 wherein the temperature in step [[i)(d)]] (c) is ~~preferably~~ in the range of –35°C to –50°C.

25. (Currently Amended) A process according to claim 1 wherein the mixed acid anhydride is condensed with protected 7-amino-3- (propen-1-yl)-3-cephem-4-carboxylic acid ~~7-APCA~~ at a temperature ~~preferably~~ in the range of –90° to –30°C.

26. (Currently Amended) A process according to claim [[1]] 25 wherein the mixed acid anhydride is condensed with protected 7-amino-3- (propen-1-yl)-3-cephem-4-carboxylic acid ~~7-APCA~~ at a temperature ~~most preferably~~ in the range of –50° to –40°C.

27. (Currently Amended) A process according to claim [[25]] 38 wherein the mixed acid anhydride is condensed with protected 7-amino-3- (propen-1-yl)-3-cephem-4-carboxylic acid ~~7-APCA~~ at a temperature ~~most preferably~~ in the range of –50° to –40°C.

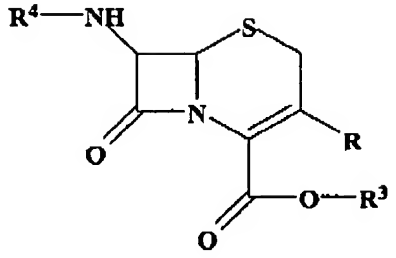
28. (Currently Amended) A silylated 7-amino-3- (propen-1-yl)-3-cephem-4-carboxylic acid ~~compound of~~ according to claim 4, is of formula (VI)[[.]]



(VI).

29-30. (Canceled)

31. (New) A process according to claim 3 wherein the protected 7-amino-3- (propen-1-yl)-3-cephem-4-carboxylic [7-APCA] of formula (VII) used



(VII)

is such that R^3 and R^4 are each tri alkylsilyl group, and R is propen-1-yl.

32. (New) A process according to claim 7, wherein the polar aprotic solvent is N, N-dimethyl formamide.

33. (New) A process according to claim 8, wherein the polar aprotic solvent is N, N-dimethyl formamide.

34. (New) A process according to claim 41, wherein the suitable acylating agent is ethyl chloroformate.

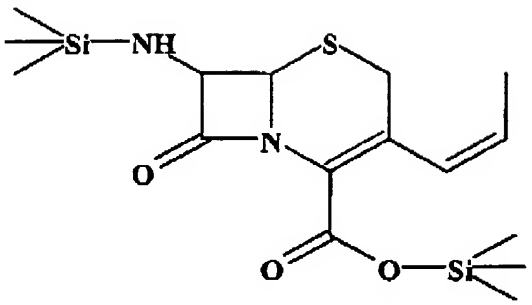
35. (New) A process according to claim 42, wherein the suitable acylating agent is ethyl chloroformate.

36. (New) A process according to claim 11, wherein the base is N-methylmorpholine.

37. (New) A process according to claim 12, wherein the base is N-methylmorpholine.

38. (New) A process according to claim 3, wherein the mixed acid anhydride is condensed with protected 7-amino-3-(propen-1-yl)-3-cephem-4-carboxylic acid at a temperature in the range of –90° to –30°C.

39. (New) A silylated 7-amino-3- (propen-1-yl)-3-cephem-4-carboxylic acid according to claim 31, is of formula (VI)



(VI).

40. (New) A process according to claim 3 wherein the temperature in step (d) is in the range of –35°C to –50°C.

41. (New) A process according to claim 9 wherein the suitable acylating agent is selected from the group consisting of chloroformic acid, benzoic acid, pivalic acid, 2-ethylhexanoic acid, ethyl chloroformate, isobutyl chloroformate, pivaloyl chloride, 2-ethyl-hexanoyl chloride, and benzoyl chloride.

42. (New) A process according to claim 10 wherein the suitable acylating agent is selected from the group consisting of chloroformic acid, benzoic acid, pivalic acid, 2-ethylhexanoic acid, ethyl chloroformate, isobutyl chloroformate, pivaloyl chloride, 2-ethyl-hexanoyl chloride, and benzoyl chloride.